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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/674,228	09/29/2003	Samir M. Hanash	108140.00015	1891

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EXAMINER	
REDDIG, PETER J	
ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
10/10/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

NYIPDocket@arentfox.com
Patent_Mail@arentfox.com

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/674,228	**Applicant(s)** HANASH ET AL.	
	Examiner PETER J. REDDIG	**Art Unit** 1642	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 27 August 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,2 and 4*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Karen A Canella/
Primary Examiner, Art Unit 1643

Continuation of 11. does NOT place the application in condition for allowance because: Applicants argue that Hirsch et al. is cited for disclosing a method of identifying proteins that induce antibodies in Hodgkin's disease (i.e., lymphoma) by isolating proteins from cancer cells derived from Hodgkin's disease patients, subjecting the isolated proteins to 2D PAGE followed by Western blot analysis with sera from cancer patients as compared to normal control patients. The proteins bound by antibodies present in serum of cancer patients, but not in serum of normal patients, are identified as proteins to which a subject with cancer produces antibodies and a subject without cancer does not.

Applicants argue that Hirsch et al. performs a method for screening antibodies in serum samples from patients afflicted with Hodgkin's disease in which the serum proteins are first subjected to 1D gel electrophoresis and western blotting to identify a particular polypeptide. The samples are then used in 2D immunoblotting to further characterize the previously-identified polypeptide. The prior knowledge derived from the 1D electrophoresis is necessary for Hirsch et al. to perform all subsequent steps of the method disclosed therein, in which 2D immunoblotting is used to further characterize the peptide.
Applicants argue that one of ordinary skill in the art, having the disclosure of Hirsch et al., would conclude that 2D western blots may only be interpreted by having a priori knowledge of the protein of interest derived from first performing 1D electrophoresis.
Applicants argue that the presently-claimed invention provides a means, previously not available, for performing 2D western blots to discover proteins to which patients with cancer raise autoantibodies, where individuals without cancer do not, without prior knowledge of the proteins to be so identified.

Applicants arguments have been carefully considered, but have not been found persuasive because the interpretation of the 2D western blots does not require a priori knwoledge about the protein. One of skill in the art at the time the invention was made could interpret the 2D western blot analysis with reasonable expectation of success given that 2D gel electrophoresis was routinely used at the time the invention was made for protein identification as evidence by the combined teaches of Hirsch et al. and Krska et al and 2D gel electrophoresis provides better definition of the protein to be identified as it determining both the molecular weight and pI of the unknown protein.

Applicants argue that the outstanding rejections based on Hirsch et al. ignore the fact that Applicants' claims recite a method "consisting of' steps (a) through (f). It is well-settled that the transitional phrase "consisting of" excludes any element, step, or ingredient not specified in the claim. See MPEP 2111.03. Applicants argue that the method disclosed in Hirsch et al., in which an initial 1D electrophoresis must be performed to interpret the results of a subsequent 2D immunoblot, does not disclose or suggest the presently-claimed invention, in which a 2D immunoblot is used to discover proteins to which patients with cancer raise autoantibodies, where individuals without cancer do not, without prior knowledge of the proteins to be so identified. Applicants argue that one skilled in the art would not be motivated to modify the techniques disclosed in Hirsch et al. by eliminating the 1D electrophoresis step to arrive at the presently-claimed invention, and there is no suggestion in the prior art that such a modification would produce a useful result.
Applicants argue that these deficiencies of Hirsch et al. are not remedied by further combination with Krska et al., which is cited for allegedly disclosing a method of 2D PAGE followed by western blotting analysis.

Applicants arguments have been carefully considered, but have not been found persuasive because Hirsch et al. do not teach that the initial 1D electrophoresis must be performed to interpret the results of a subsequent 2D immunoblot. Given the conventional nature of 2D immunoblot analysis at the time the invention was made, given that 2D gel electrophoresis provides better definition of the protein to be identified as it is determining both the molecular weight and pI of the unknown protein, and given that the elimiation of the 1D gel step would expedite the process without affecting the outcome, it would be obvious to perform the 2D immunoblot analysis of Hirsch et al. or Krska et al. to identify cellular protein antigens to which a subject with cancer produces autoantibodies and a subject without cancer does not, without prior knowledge of the proteins being identified at the time the invention was made.

Applicants argue that the key difference between the presently-claimed invention and the cited references is that the combination of Krska et al. and Hirsch et al. requires a priori knowledge of the protein of interest before western blot patterns can be interpreted, whereas the presently claimed invention permits the discovery of proteins without prior knowledge of the proteins to be so identified. Krska et al. does not disclose a method consisting of Applicants' steps (a) through (f), and does not provide any suggestion or motivation to modify the disclosure of primary reference Hirsch et al. to eliminate the 1D electrophoresis step to arrive at Applicants' presently claimed invention.
Applicants argue that the Office Action is improperly interpreting the claims in order to maintain the rejections based on Hirsch et al. and Krska et al. Applicants argue that specifically, the Office Action apparently continues to read the claims as being directed to a method "comprising" Applicants' claimed steps (a) through (f), rather than the presently-claimed methods which consist of Applicants' claimed steps (a) through (f).
Applicants argue that accordingly, the combination of Hirsch et al. and Krska et al. fails to disclose or suggest the presently-claimed method, and nothing in their disclosures would lead one skilled in the art to modify them without the benefit of hindsight reconstruction based on Applicants' disclosure.

Applicants arguments have been carefully considered, but have not been found persuasive because the 2D electrophoresis Hirsch et al. clearly could be used to identify unkown proteins at the time the invention was made and Hirsch et al. do not teach away from using it alone. Given that elimination of the 1D gel would make the method more efficient without comprising its accuracy as both methods identify the same protein antigen to which the antibodies bind and given that there were a finite number of predictable methods in the art for identification of proteins antigens at the time the method was made, one of skill in the art would have been motivated with a reasonable expectation of success to combine the teachings of Hirsch et al. and Krska et al. and perform the 2-D electorphoresis immunoblot to identify cellular protein antigens to which a subject with cancer produces autoantibodies and a subject without cancer does not, without prior knowledge of the proteins being identified at the time the invention was made.